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Use of Tranexamic Acid to reduce intraoperative bleeding in Craniotomy for meningioma Patients

Ahsan Khaliq Siddiqui, Rajesh Raman, Zia Arshad, MD, Hemlata, Satish Varma, Ahmad Suhaeb Hashmi,

Abstract

Background:

Intraoperative blood loss is always a concern to anaesthesiologist. Blood loss in neurosurgery may cause major complication require blood transfusion. The purpose of this study was to assess the effect of tranexamic acid (TXA) on intraoperative and postoperative blood loss and other benefit of tranexamic acid on output of meningioma surgery.

Material and Method:

This study is a prospective, randomized and double-blinded study conducted in department of Neurosurgery, King George Medical University, and Lucknow, India from January 2017 to January 2018. A total of 100 patients aged 15-75 years, with American Society of Anaesthesiologists physical Status 1 and 2 scheduled to undergo elective craniotomy for meningioma excision were enrolled. Patients were divided into two groups. Each group received either 2 gram of tranexamic acid in 50 ml normal saline or 50 ml normal saline with placebo just after induction of anaesthesia. We observed intra and postoperative blood loss, blood transfusion and duration of surgery, postoperative complications like nausea, vomiting, thromboembolic complications and postoperative stay in hospital.

Results: The intraoperative blood loss was significantly decreased. Need for blood transfusion also decreased in tranexamic group. This decreased blood loss caused decreased postoperative complications and stay in hospital.

Conclusion:

There is a significant reduction in the total amount of blood loss in TXA group causing reduction in intraoperative transfusion requirement and less postoperative complications and stay in hospital.

Keywords: Intraoperative blood loss; neurosurgery; meningioma; tranexamic acid (TXA)

Introduction

Meningiomas are usually benign tumors arising from the meninges of the brain and spinal cord. They represent about one-third of all primary brain tumors. With the help of modern surgical equipment and skin holding clip, blood loss in meningiomas is not a major issue. But sometimes

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blood loss is causing complication in neurosurgery that requires transfusion of multiple units of blood.[1] Tranexamic acid is used to treat or prevent excessive blood loss from trauma, surgery, and in various medical conditions including hemophilia and heavy menstrual bleeding. In other words Tranexamic acid is an antifibrinolytic. It works by preventing blood clots from breaking down too quickly. This helps to reduce excessive bleeding during various surgeries and dental extractions in haemophiliacs .[2, 3] Tranexamic acid can be used as local or as general fibrinolytic. As local fibrinolytic, tranexamic Acid can be used in prophylaxis and treatment in patients at high risk of per and post-operative haemorrhage following prostatectomy, conisation of the cervix, surgical procedures. For general fibrinolysis, tranexamic acid is used in haemorrhagic complications in association with thrombolytic therapy or haemorrhage associated with disseminated intravascular coagulation with predominant activation of the fibrinolytic system. Recently its indication has been extended to decrease blood loss in various type of surgeries with expected more blood lose i.e. spinal surgeries, gynaecological surgeries, oncosurgeries, orthopedic surgeries specially arthoplasty, cardiac surgery. Recently the use of tranexamic acid has been extended to Neurosurgery. Meningiomas usually grow inward, causing pressure on the brain or spinal cord. They can also grow outward, towards the skull, causing it to thicken. Most meningiomas are noncancerous, slow-growing tumors. Some contain sacs of fluid (cysts), mineral deposits (calcifications), or tightly packed bunches of blood vessels. These blood vessels may bleed some time profusely.

Tranexamic acid is frequently used following major trauma.[4] Tranexamic acid comes in oral and intravenous forms. It should be given very slowly intravenously. Injections should not be administered by the intramuscular route. To achieve local fibrinolysis, the recommended standard dose is 5-10ml (500-1000mg) by slow intravenous injection (1 ml/min), three times daily. Following an initial intravenous injection, subsequent treatment may proceed by intravenous infusion. In spinal surgeries like scoliosis surgery, Tranexamic Acid could be used up to 4-5 gram. In such spinal surgeries, after giving 500-1000 mg bolos, further dose may be administered at a rate of 10-20 mg/kg body wt/hour throughout the surgery.

The efficacy and safety of Tranexamic acid in children undergoing surgery have not been fully established. In elderly patients there is no need to reduce dosage unless there is evidence of renal failure. Due to the risk of cerebral oedema and convulsions, intrathecal or intraventricular injection and intracerebral application are contra-indicated. In patients with a history of convulsion, tranexamic acid should not be administered. In case of haematuria of renal origin, there is a risk of mechanical anuria due to formation of a ureteral clot.

SUBJECTS AND METHODS

This study is a prospective, randomized and double-blinded study conducted in department of Neurosurgery, King George Medical University, Lucknow, UP, India from January 2017 to January 2018 after obtaining the ethics committee approval from King George Medical University Ethics Committee. After obtaining written inform consent, we took 100 patients in age group from 15-75 years, belonging to American Society of Anaesthetist 1 and 2 physical status of either sex, admitted for elective intracranial meningioma excision surgery. Patients with hepatic and renal disorders, with bleeding diathesis/abnormal coagulation parameters (abnormal prothrombin time [PT], platelet counts), patient on aspirin or any other anticoagulants and patients undergoing intracranial vascular surgeries and patients with haemoglobin less than 10 gram% were excluded from the study. Demographic data such as sex, age and weight were noted. Patients were

randomly divided into two groups by computer generated list with 50 patients in each group. A 20 gauge cannula was placed in a dorsal vein of the non-dominant hand in pre surgical room. All the patients were premedicated with intravenous midazolam 0.10 mg/kg body weight. Fifteen minutes after premedication the patients were taken to the operating room. In the operating room all standard monitors including blood pressure (BP), oxygen saturation (SpO2), and ECG (HR and rhythm) were applied. Anaesthesia was induced with fentanyl 2 mg/ kg, propofol 2–2.5 mg/ kg body weight and rocuronium was used for relaxation. Endotracheal tube was inserted after loss of consciousness and the lungs were ventilated to maintain the end-tidal carbon dioxide partial pressure between 30-35 mmHg. Anaesthesia was maintained in both groups with sevoflurane in Oxygen and Air. It is our standard protocol to insert a CVP line in right internal Jugular vein with help of ultrasound and Arterial line in non-dominant hand were inserted after induction of anaesthesia and intubation.

Identical 50 ml syringes containing either 2 gram of Tranexamic Acid in 50 ml Normal Saline (NS 0.9%) or 50 ml NS only were prepared according to study designed. Syringes were prepared and concealed by an anaesthesia resident not involved in any other part of the study. Another anaesthesiologist blind to both groups and drug syringes allocation was responsible for application of the concealed syringes and recording all data. All 100 patients were randomly divided into two groups by computer generated list with 50 patients in each group. Group T (Tranexamic group) received 2 gram of Tranexamic Acid in 50 ml 0.9% normal saline and Group C (Control group) received only 0.9% Normal Saline 50 ml. The anaesthetic technique was standardized for all patients. Throughout the Surgery in all patients' blood pressure was maintained within 20 % of their baseline value in all patients. Blood loss was assessed by collection of blood in suction and weighting the surgical sponges used in surgery. Post-operative blood loss was assessed by seeing the blood accumulated in drain in first 24 hours postoperatively. We assessed the total intraoperative and post-operative blood loss, post-operative nausea and vomiting and postoperative stay in hospital.

Statistical Analysis

Patients' demographic, clinical and laboratory parameters were recorded. The number of patients and their demography, clinical parameters included for this study were expressed as the mean - + standard deviation and analysed by one way analysis of variance (ANOVA) test. Student`s t-test was used for comparison of normally distributed data, while Mann-Whitney U-test was used for data which did not achieve normality. Data were tested for normal distribution using the Kolmogorow-Smirow test. All statistical analysis was carried out at 5% level of significance and the p value of <0.05 was considered significant and if p value was > 0.05, it will be considered that there were no statistically significant differences between the two groups. Statistical analysis was carried out using SPSS statistical software version[16].

Result

Fifty patients in each group completed the study. There were no significant difference between both groups with respect to the demographic data and position of patients during surgery as shown in table 1. Table 2 is showing comparison between duration of surgery, total blood loss, post-operative stay in hospital, and number of patients required blood transfusion.

The total blood loss in the group T (Tranexamic Acid group) was 469-+ 117.75 ml which is much less than the blood loss in Control group (Group C) where the blood loss was 672-+184.37 ml. Duration of surgery was also significantly decreased in group T with comparison to group C. In group T, duration of operation was 4.10-+0.72

hours whereas 4.66-+0.78 hours. The post operation stay in hospital was also less in group T when compare it to group C, 6.44-+1.65 days in group-T and 8.48 days in group-C, which is also significant. Total number of patients required blood transfusion whether intra-operative or postoperative in group T was also significantly less than Control group.

In table-3 we compare postoperative complications in terms of postoperative blood loss in drain, number of patients developed Nausea and Vomiting, Seizer activity, thromboembolic complications and post-operative mortality within 48 hours of operation. We found that there is no significant deference in both group.

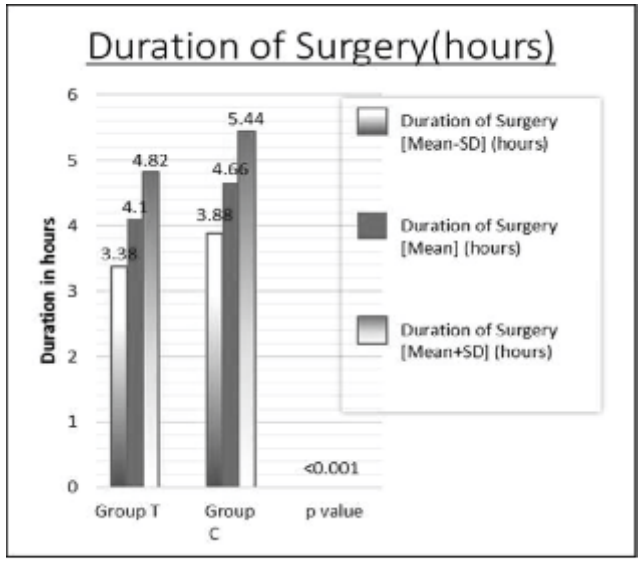
Table 1 - Patient characteristics in each group. Age and weight data are expressed in Mean ±SD

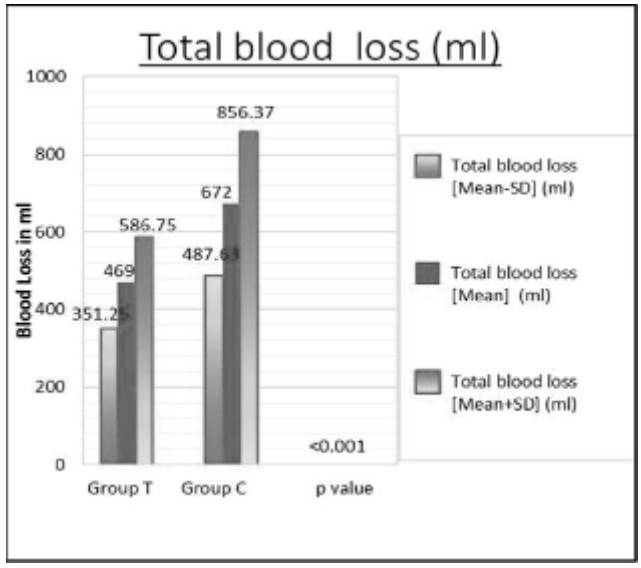
	Group T	Group C	p value
Age (Yr.)	50.1±14.62	49.44±14.36	0.820 (p>0.05)
Weight (KG)	68.7±16.98	68.54± 16.22	0.961 (p>0.05)
Male /Female	28/22	32/18	p > 0.05
ASA status (I&II)	40/10	40/10	p > 0.05
Position during Surgery (Supine/ prone)	38/12	41/9	

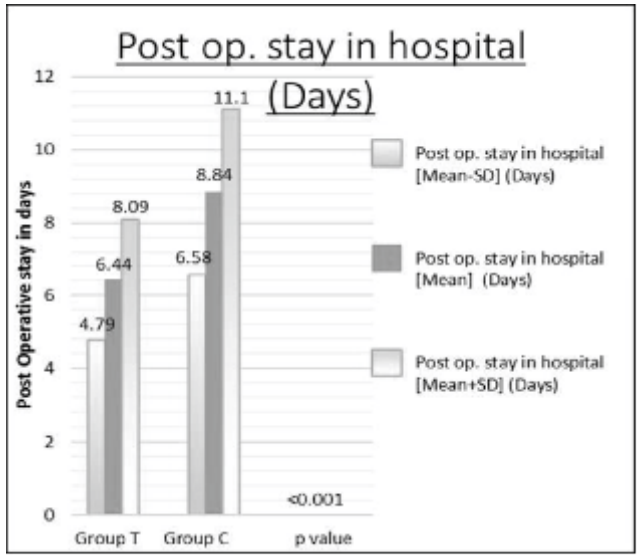
ASA- American Society of Anaesthesiologists, SD – Standard deviation

Table 2 – Comparison between duration of surgery, total blood loss, post-operative stay in hospital, and number of patients who required blood transfusion (data are in Mean ±SD)

	Group T	Group C	p value
Total blood loss (ml)	469 ± 117.75	672±184.37	P < .001
Duration of Surgery (hours)	4.10 ± 0.72	4.66 ± 0.78	P < .001
Post op. stay in hospital (Days)	6.44±1.65	8.84±2.26	P < .001
No. of patients required transfusion	7	12	







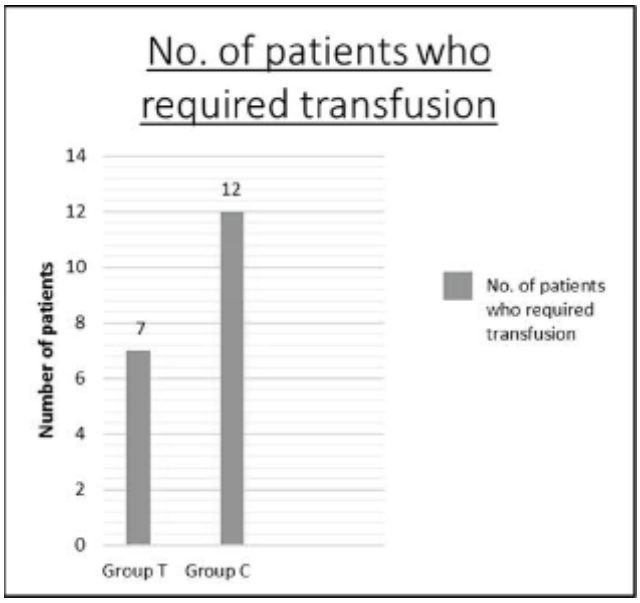


Table 3- Post operative complication and mortality in 48 hours.

	Group T	Group C
Post-operative blood loss		not significant
Patients develop Nausea/ vomiting post operative	12	14
Seizure activity	4	4
Thromboembolic Complications	Nil	Nil
Post-operative mortality within 7 days	2	3

Discussion

We anaesthetists are always trying to decrease intraoperative blood loss by using various techniques like decreasing the mean blood pressure, controlling the depth of anesthesia and using adequate relaxation. We know that the transfusion of homologous blood and blood products are exposing the patients to risks of infectious disease transmission, transfusion reaction, and immunosuppression.[5,6] Furthermore, replacement of massive intraoperative bleeding with crystalloids and packed erythrocytes during the surgery can dilute the coagulation factors and further increase surgical bleeding.[7]

Several scientific studies to reduce blood loss and transfusion requirements have been done.[8,9,10,11,12,13] However, none of these scientific research and strategies are free of complications. Hemodilution and controlled hypotension may compromise tissue oxygen delivery during rapid blood loss.[14]

Here, the purpose of our study was to assess the effectiveness of tranexamic acid, an antifibrinolytic drug, on intraoperative and post-operative blood loss and blood transfusion in patients undergoing craniotomy for meningioma (tumor) excision. We observed that the intravenous administration of tranexamic acid caused significant decrease in intraoperative and postoperative blood loss. This decreased blood loss is responsible for less intraoperative and postoperative blood transfusion, decrease duration of surgery and post operarive complications like postoperative nausea and vomiting and less postoperative stay in hospital. We know that tranexamic acid (Trans 4 amino methyl cyclohexane carboxylic acid), an antifibrinolytic drug, inhibits the conversion of inactive plasminogen to the active proteolytic enzyme plasmin by competitively blocking of high affinity lysine binding site of plasminogen.[15] This prevents plasmin from binding to fibrinogen and fibrin structures after clot formation and decrease oozing and blood loss from operative site.

Previous studies are showing that tranexamic acid is found to decrease blood loss significantly in major orthopaedic surgeries. Four relevant prospective, randomised studies have shown a reduction of about 50% in both the postoperative blood loss and the need for blood transfusion on the first postoperative day in patients who received prophylactic tranexamic acid when operated on for a total knee replacement.[16]

In Spinal surgeries, studies have shown a significant reduction in intraoperative bleeding. The requirement for blood transfusion when they used tranexamic acid, aminocaproic acid,

aprotinin, and recombinant activated factor VII just preoperative or intraoperatively, tranexamic acid was showing better results.[17] In spine surgery, e.g. scoliosis correction with posterior spinal fusion using instrumentation, to prevent excessive blood loss tranexamic acid was found very effective.[18]

The safety and efficacy of the antifibrinolytic, tranexamic acid in elective neurosurgical procedures is not well known. Complex skull base neurosurgery has the potential for increased intraoperative blood loss and coagulation near eloquent cranial structures should be minimized. Mebel D et al. Published a study in 1999 on complex skull base neurosurgery and use of tranexamic acid. The primary objective was to determine the relationship between the use of tranexamic acid and transfusion at our institution. Their results demonstrate that tranexamic acid use is associated with reduced transfusion rates in their study population, with no apparent increase in seizure or thrombotic complications. The author emphasized the need for further randomized clinical trials to evaluate the efficacy and safety of tranexamic acid on perioperative blood loss during complex skull base neurosurgery.[19]

The clinical randomization of an antifibrinolytic in significant haemorrhage (CRASH-2) trial in potential head injury patients, published in 2010, assessed the effect of early administration of tranexamic acid to adult patients with trauma with or without risk of significant haemorrhage within 8 hours of injury. This trial showed significant reduction of all-cause mortality with no increase in vascular occlusive events. [20]

To quantify the effect of TXA on intracranial haemorrhage, the CRASH-2 Intracranial Bleeding Study evaluated 270 adult patients with TBI (traumatic brain injury) out of 20,211 trauma patients recruited in the CRASH-2 trial.[21] There was a reduction in intracranial haemorrhage growth, ischemic lesions and mortality in TXA allocated patients, but these results were statistically insignificant showing neither moderate benefits nor harmful effects of TXA in traumatic brain injuries (TBI) patients. Results of ongoing CRASH-3 will reliably determine the effectiveness of early administration of TXA in TBI patients.[22] In surgical corrections of craniosynostosis in children it reduces the need for blood transfusions. In another study, the aim of the study is to estimate clinical effectiveness of fibrinolysis inhibitor, Tranexamic Acid in neurosurgical patients with intracranial tumors. To study hemostasis: APPT, PT index, TT, fibrinogen, ATIII activity, factor XII-derived fibrinolysis, spontaneous euglobulin lysis. In this study, the use of Tranexamic Acid caused significant decrease of fibrinolytic activity and bleeding reduction from the wound. The duration of surgical haemostasis in the tranexamic acid group is significantly lower than in the control group. Drainage blood loss was lower in the main group than in the control group. Thus Tranexamic acid decreases the risk of intraoperative blood loss in the patients with brain tumors.

In another study, Novikov VIu and Kondrat'ev AN estimated the clinical effectiveness of Tranexamic Acid in neurosurgical patients with intracranial tumors. Tranexamic Acid injection during diffuse bleeding from small vessels led to quick and visible bleeding reduction. Thus Tranexamic Acid decreases the risk of intraoperative blood loss in the patients with brain tumors. [23]

In terms of intravenous thromboembolic complications during and after the TKA operation, a short-term use of TXA can significantly decrease blood loss and blood transfusion with no increasing risk for venous thrombosis.[24] The author investigated the effect of treatment with TXA, on blood loss, blood transfusion requirements and blood coagulation. Coagulation profile was examined (bleeding time, platelet count, prothrombin time (PT), activated partial

thromboplastin time (aPTT), plasminogen, beta-thromboglobulin and fibrinogen). Fibrinolysis was evaluated by measurement of concentrations of D-dimer and fibrinogen degradation products (FDP). Total blood loss in the TXA group was significantly less during surgery. Postoperative packed cell volume values were higher in the TXA group despite fewer blood transfusions. Postoperative concentrations of plasminogen were decreased significantly in the tranexamic acid group ($P < 0.001$). Platelet count, PT, aPTT, bleeding time, beta-thromboglobulin, fibrinogen and FDP concentrations did not differ between groups, but D-dimer concentrations were increased in the control group. Thromboembolic complications were similar in both groups. [25]

When the safety and efficacy of tranexamic acid (TXA) in total knee arthroplasty (TKA) and total hip arthroplasty (THA) was evaluated in a meta-analysis for total blood loss, the incidence rate of deep vein thrombosis (DVT) and pulmonary embolisms (PE) was not significant and the number of patients requiring at least 1 unit of red blood cell following surgery was also significantly less. It suggests that the use of TXA reduced the risk of blood loss and the need for allogeneic blood transfusion significantly, without apparent increased risk of DVT or PE complications.26 In a systematic review and meta-analysis study of randomised controlled trials evaluating the effect of tranexamic acid (TXA) upon blood loss and transfusion in primary total knee replacement, Subgroup analysis of high-dose (> 4 g) TXA showed a plausible consistent reduction in blood transfusion requirements. The current evidence from trials does not support an increased risk of deep-vein thrombosis or pulmonary embolism due to TXA administration.[27] Keeping in mind this meta-analysis in our study we have chosen 2 gram of TXA as our study dose. For thrombotic risks of TXA use in non-cardiac surgery more studies and clinical trials are needed. Patients with any hypercoagulable risk factors, including HIV infection or any prior thrombotic history in which TXA use is being considered, should prompt a discussion among the perioperative physicians involved.[28] Hence, TXA use in this context is still an area of uncertainty, and its thrombogenic risks are yet to be studied as a primary outcome in any large prospective trial to date.

Conclusion

Significant reduction in the total amount of blood loss in TXA group is responsible for significant reduction in intraoperative blood transfusion requirement.

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Dexmedetomidine as an adjuvant to bupivacaine in brachial plexus block: Prospective, randomized, double blind study.

Syed Hussain Amir, Qazi Ehsan Ali, Shaista Jamil

Abstract

Objective: Use of adjuvants to regional blocks has been in vogue in the recent past. Several adjuncts have been studied to potentiate the efficacy of local anesthetics in brachial plexus block but dexmedetomidine has sparingly been used as an adjuvants. We studied this drug as a sole adjuvant to local anaesthetic bupivacaine in brachial plexus block.

Method

The patients were divided into two groups of 25 patients each. In Group A, 30 ml of 0.5 % bupivacaine with 1 ml normal saline was given for brachial block whereas in Group B, 30 ml of 0.5 % bupivacaine with 1 ml dexmedetomidine (100 µg) was injected. Primary outcome method was onset and duration of sensory and motor block whereas secondary outcome measures were pain scores, requirement of analgesics and haemodynamic changes.

Result

Sensory onset time was 5.76± 2.47 minutes in Group B which was significantly less than group A whereas it was 10.44±3.57minutes. Also onset of motor blockade in Group A was 16.76±4.78 minutes and in Group B was an 11.24±3.81 minute which was statistically significant. The mean duration of analgesia for Group A was 525.4±124.99 minutes and for Group B it was 712.8±103.78 minutes. The mean duration of motor blockade for Group A is 469.8±122.68 minutes and for Group B is 669. 4 ±105.33 minutes which was also statistically significant.

Conclusion

Dexmedetomidine as an adjuvant to bupivacaine significantly shortens the onset time of sensory and motor block in brachial plexeus block. Also total duration of analgesia and motor blockade is prolonged when dexmedetomidine is added to bupivacaine and the requirement for analgesic drugs in the postoperative period is also decreased.

Keywords

Dexmedetomidine; Brachial plexeus; Sensory block, Motor block

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Abstract

Objective: Use of adjuvants to regional blocks has been in vogue in the recent past. Several adjuncts have been studied to potentiate the efficacy of local anesthetics in brachial plexus block but dexmedetomidine has sparingly been used as an adjuvants. We studied this drug as a sole adjuvant to local anaesthetic bupivacaine in brachial plexus block.

Method

The patients were divided into two groups of 25 patients each. In Group A, 30 ml of 0.5 % bupivacaine with 1 ml normal saline was given for brachial block whereas in Group B, 30 ml of 0.5 % bupivacaine with 1 ml dexmedetomidine (100 µg) was injected. Primary outcome method was onset and duration of sensory and motor block whereas secondary outcome measures were pain scores, requirement of analgesics and haemodynamic changes.

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INTRODUCTION

A peripheral nerve block is the injection of a local anaesthetic around a nerve or group of nerves with blockade of nerve impulse conduction, causing temporary analgesia and loss of sensory and motor function. Peripheral nerve blocks are cost effective anaesthetic techniques used to provide superb anaesthesia and analgesia while avoiding airway instrumentation and the hemodynamic consequences of general and neuraxial anaesthesia[1].

Satisfactory surgical conditions are obtained with complete sensory and motor blockade. Concurrent sympathetic blockade reduces post-op pain, vasospasm and oedema[2,3]. The bupivacaine which is an amide local anaesthetic is the most frequently used local anaesthetic [2,3].

Several adjuncts have been studied to potentiate its efficacy including opioids, midazolam, neostigmine, bicarbonate, hyaluronidase and α-2 agonists[4-11]. The use of a-2 adrenoceptor agonist for enhancement of peripheral nerve blocks has added a new dimension to their clinical application[12]. Clonidine, when combined with a local anaesthetic has been found to extend the duration of nerve block[13]. Dexmedetomidine is the most recent agent in this group approved by FDA in 1999 for use in humans for analgesia and sedation. Dexmedetomidine, a highly selective potent a-2 agonist, an imidazole compound is pharmacologically active dextroisomer of medetomidine. Dexmedetomidine, when combined with a local anaesthetic, has been found to extend the duration of nerve block[14-16]. It has been postulated that this action could be due to local vasoconstriction, facilitation of C fiber blockade, activation of the receptors in the brain and spinal cord inhibits neuronal firing, causing hypotension, bradycardia, sedation, and analgesia[17].

METHODS

After Institutional ethical committee approval and written informed consent, a double blind randomized prospective clinical study was carried out on 50 American society of anaesthesiologists (ASA) grade I & II adult patients of either sex, aged 18-60 years, undergoing upper limb surgery under supraclavicular brachial plexus block. Patients receiving anticoagulants, β- blockers or opioids, patients with history of hypertension, myocardial infarction, alcohol abuse, pregnant patients, psychiatric history, diabetes mellitus, contra lateral phrenic nerve palsy, neurological deficit, peripheral neuropathy or hypersensitivity to local anesthetic agents,were excluded from the study.

The patients were divided randomly into two groups, using computer generated table. Group A patients received 30 ml of 0.5 % bupivacaine with 1 ml normal saline whereas 30 ml of 0.5 % bupivacaine with 1 ml dexmedetomidine (100 µg) were given in Group B patients.

Before shifting the patient to the operation theatre, an intravenous access was obtained and routine monitors were attached. Then inj. Ondansetron 4 mg i.v. was given.

All the patients received brachial plexus block through the supraclavicular approach. Neural localization was achieved by using a nerve locator connected to 22 G, 50 mm- long stimulating needle (stimuplex).Persistence of contraction with stimulator voltage decrease to 0.5 Ma was taken as the confirmation of the brachial plexus. The needle was then held immobile and 1ml of the local anaesthetic injected. At this point the twitching should disappear. The mechanism for the immediate disappearance of the twitching is not a result of the local anaesthetic blocking the nerve, but the mechanical displacement of the nerve away from the needle tip[18]. So, after confirming the needle tip is not inside a nerve or a vessel, rest of the drug was injected, after negative aspiration every two to three ml. patients of either group (n =25 each) were given either 1 ml (100µg) of dexmedetomidine (group B) or 1ml of normal saline (group A) along with 30 ml of 0.5 % bupivacaine. The nature of drug or group of the patient was not known to the one performing the block. Inj. Midazolam 0.01- 0.1 mg/kg i.v. was given to the patient once complete block had been confirmed.

We defined the successful block as one that allows the surgery to proceed within a 30 minute time period, without discomfort to the patient or need for any supplemental techniques.
All the patients were observed and values recorded meticulously for the following effects both in intraoperative and in the post-operative period.

Primary outcome method was onset and duration of sensory and motor block whereas secondary outcome measure was pain scores.

Sensory block was assessed by pin prick method. Sensory onset was considered when there was a dull sensation to pin prick. Complete sensory block was considered when there was complete loss of sensation to pin prick. Assessment of sensory block was done at each minute after completion of drug injection till complete sensory blockade.

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. Motor blockade was evaluated by the ability to flex the elbow and hand against gravity as Grade 1(Ability to flex and extend the forearm),Grade 2(Ability to flex or extend only the wrist and finger, Grade 3 (Ability to flex or extend only the fingures) and Grade 4 (Inability to move the forearm, wrist, fingers).The block was considered to be incomplete when any of the segments supplied by median, radial, ulnar and musculocutaneous nerve did not have analgesia even after 30 min. of drug injection.

when more than one nerve remained unaffected, the block was judged to have failed. In this case general anesthesia was given. Patients were monitored for hemodynamic variables such as heart rate, blood pressure and oxygen saturation every 15 min after the block intraoperatively and every 60 min post operatively for 24 hours.

Duration of sensory block was defined as time from injection of drug to appearance of pain, requiring analgesia. Pain was assessed on a rating scale, zero representing no pain and 100 meaning worst possible pain. Injection tramadol 2mg/kg i.v. was given as rescue analgesic when the pain score was more than 40. Pain scores were recorded at thirty minutes, two hours and at eight hours after the surgery.

Duration of motor block: it was defined as time from injection of drug till complete return of motor power.

The collected data were analysed using Windows Microsoft excel 2007 version and Graphpad software prism 6.

Patient's demographic data were analysed using unpaired t -test. Pain Scores was analysed using chi square test. The difference was considered statistically significant at a p value of <0.05 with 95% confidence interval.

RESULTS

Both the groups were comparable in terms of age, gender, weight and type of surgeries. (Table 1). Mean Sensory onset time in Group A was 10.44±3.57minutes (Table 2) and in Group B was 5.76± 2.47 minutes which was statistically significant.

Onset of motor blockade in Group A was 16.76±4.78 minutes and in Group B was an 11.24±3.81 minute which was also statistically significant (p <0.0001).

The mean duration of analgesia for Group A was 525.4±124.99 minutes and for Group B it was 712.8±103.78 minutes.

The mean duration of motor blockade for Group A was 469.8±122.68 minutes and for Group B was 669.4±105.33minutes(Table 2). The difference in the duration of analgesia and motor blockade was statistically significant with a p value of <0.0001for both.

DISCUSSION

In this randomized double-blinded study, we studied the efficacy of Dexmedetomidine as an adjuvant to bupivacaine in peripheral nerve stimulator PNS guided supraclavicular brachial plexus block. The addition of 100µg dexmedetomidine to (PNS) guided supraclavicular brachial plexus block increased the duration of both sensory and motor blockade and the need for analgesic in postoperative period was also reduced significantly.

In 2010 work has been done on similar line by Aliye Esmaoglu et al[16] who added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shortens the onset time of both sensory and motor block, prolongs the duration of block and the duration of post-operative analgesia. In 2012 Sarita S swami et al. compared clonidine vs. Dexmedetomidine as an adjuvant to 0.25% bupivacaine and reported that the onset of sensory block was faster in dexmedetomidine group.

In 2012 Rachna Gandhi et al[19] reported that onset of motor and sensory blockade was faster in control Group as compared to dexmedetomidine group. But no convincing explanation for their finding could be given. It may be because of the different dose of dexmedetomidine used by them.

In our study as well as in various other studies onset of sensory and motor block was shortened in dexmedetomidine group.

Addition of dexmedetomidine to local anaesthetic in brachial blocks significantly prolonged the

duration of sensory (analgesia) and motor blockade in our study as well as the studies done previously by others. The mechanism by which 2adrenergic receptor agonists produce analgesia and sedation is not fully understood, but is likely to be multifactorial. Peripherally, a2 agonists produce analgesia by reducing release of nor epinephrine and causing a2 receptor-independent inhibitory effects on nerve fibre action potentials. Centrally a2 agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of a2 adrenoceptors in the locus coeruleus.[20,21] Moreover, experiments on dexmedetomidine as an adjuvant for nerve blocks have shown that the duration of analgesia is prolonged by block of the hyper polarization-activated cation current (Ih current).[22] The Ih current is important to bring a peripheral nerve back to the resting potential. The action potential will result in a hyperpolarized state, and the nerve will hardly be able to produce a new action potential.

Therefore, the nerve is refractory to further stimulation. To produce another action potential, the nerve needs to get back to the resting potential. This process occurs in the late phase of the repolarization period. Blocking the Ih current will result in prolonged hyperpolarization of the nerve, which seems to be more distinct in the unmyelinated C fibres (pain) than in motor fibres. Therefore, blocking the Ih current may have a more pronounced effect on pain than on motor response.[23] However, further studies are warranted to investigate the mechanisms of how an Alpha-2 agonists, and especially dexmedetomidine, prolong the action of local anesthetic in peripheral nerve blocks.

Several studies have found dexmedethomidine to be safe and effective in various neuraxial and regional anesthetics in humans, including intrathecal and IV regional anesthesia.[(24,25)] Intrathecal dexmedetomidine in combination with bupivacaine have been studied in human beings without any postoperative neurological deficit. [26]

A dexmedetomidine–lidocaine mixture has been used to provide Bier's block and was shown to improve the quality of anesthesia and tourniquet pain and reduce postoperative analgesic requirement.[24,25] Another study compared the effect of adding either clonidine or dexmedetomidine to lidocaine during Bier's block and reported that adding dexmedetomidine to lidocaine during Bier's block is superior in quality of anesthesia, tourniquet tolerance, and intraoperative and early postoperative analgesia than is the addition of clonidine.[27] Brummet et al.[28] reported that large-dose dexmedetomidine enhances the duration of bupivacaine anesthesia and analgesia of the sciatic nerve block in rats. In addition, they histopathologically showed that the nerve axon and myelin were normal in both groups at 24 hours and at 14 days. Same authors in another experimental study reported that clinically relevant doses of dexmedetomidine enhanced blockade when added to ropivacaine [(29)]

Kaslo et at.[30] reported that dexmedetomidine affinity to 2adrenoceptor agonists is 10 times as compared to clonidine when dexmedetomidine is added to lidocaine for intravenous regional anaesthesia, it has been studied that it improves quality of anaesthesia and intraoperative and postoperative analgesia without causing side effects[31-33]. However, dexmedetomidine also may lead to bradycardia.

The result in this study showed that sensory block tended to last longer as compared to motor block which agrees with the observation by De Jong et al[4]. These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block[4].

The effect of the procedure on the hemodynamic was also studied in both the groups in this study. Pulse rate and mean arterial blood pressure were recorded and compared at specified intervals i.e. pre-operative, at five minutes, thirty minutes and two hours after the block, then post operatively at thirty minutes, two hours, eight hours and twenty four hours. The mean pulse rate and mean MAP in Group A and B were comparable, preoperatively and at 5 min after block with no statistically significant difference.

The mean pulse rate and mean of MAP were significantly lower in Group B than those in Group A at 30 minutes, 2 hours and in postoperative period. The difference was statistically significant. Mean pulse rates and mean of MAP, before and after the block were also compared separately in both Group A and Group B to know the effect of respective drugs; especially the dexmedetomidine on pulse rate and blood pressure by using the paired t-test.

The comparison was made between preoperative values of mean pulse rate and mean MAP (mm Hg) with mean values at five minutes, thirty minutes and two hours after the block, then post operatively at thirty minutes, two hours, eight hours and after twenty four hours, within Group A and Group B separately.

In Group A, the values for both pulse rate and MAP were found to be statistically significant in two pairs only. At five minutes after the block, the mean pulse rate was 91.00±6.3 per minute, and mean MAP was95.84±3.63 mm of Hg in comparison to pre operative mean pulse rate of 85.84±7.52 per minute and mean MAP of 93.68± 6.10 mm of Hg and at 8 hrs mean pulse rate was 90.36±5.82 per minutes and mean MAP was 96.24±3.19mm of Hg. Both the values were statistically significant with $p < 0.05$ at 95% confidence interval.

The increase in pulse rate and rise in MAP five minutes after the block can be attributed to anxiety and pain related to the procedure, as injection midazolam was given to the patients only after confirmation of sensory and motor blocks. The same reason, i.e. post-operative pain due to regression of sensory block can be held accountable for increase in mean pulse rate and MAP eight hours post-operatively.

In Group B, the values for both mean pulse rate and MAP were found to be statistically significant. Except at 5 minutes, intraoperatively MAP and HR values were significantly lower in Group B ($P<0.05$).

At thirty minutes after the block, mean pulse rate was 75.84± 15.41 per minute, mean MAP was 87.88± 4.41 mm of Hg in comparison to pre-op mean pulse rate of 89.08± 9.4per minute and mean MAP of 93.96 ± 6.16 mm Hg, $p = 0.0008$and $p = 0.0001$respectively. There was significant decrease in pulse rate and MAP in Group B after brachial plexus block with p value < 0.05.

This can be attributed to the effect of dexmedetomidine. Tachycardia and hypertension were not seen in this group eight hours post operatively as patients had prolonged duration of analgesia in this Group And mean pain score was 45.6±15.02 for Group A and 5.2±11.59 for Group B. The difference in pain score between the two is statistically significant with a p value of <0.0001 (<0.05) at 95% confidence interval.

As seen from the data provided above, pain scores were significantly lower in patients who received dexmedetomidine in addition to bupivacaine. Inj.Tramadol 2mg/kg was given to patients when pain scores were found to be more than 40, on a scale of zero to hundred. The number of patients who required rescue analgesic were 72 % in Group A and 4% in Group B, were significantly lower at eight hours post operatively, in Group B, with a p value of(<0.05) at 95% confidence interval.

Also the mean value of boluses of analgesic required up to 24 hr post operatively in Group A was 1.92±0.75as compared to 1.304±0.55in Group B, the difference being statistically significant at a p value of 0.0018 (<0.05) at 95% confidence interval.

Side effects such as nausea and vomiting were not seen in any patients in Groups B; however one patient in Group A experienced nausea about eight hours post-operatively. This was probably a result of repeat antibiotic injection that was administered to the patient, rather than due to the procedure or any of the drugs used for the block.

Dexmedetomidine may lead to side effects such as hypotension and bradycardia with increased dosage along with its effects such as sedation and anxiolysis [34]. In this study almost all the patients remain sedated but arousable without any sign of respiratory depression in Group B, however 3 patients in Group B were sedated in the postoperative period but their reflexes were intact. Bradycardia was seen in 8 % of the patients in Group B who responded to inj. atropine. Rest of the patients in either group had an uneventful course without major complications.

CONCLUSION

Dexmedetomidine with bupivacaine significantly shortens the onset time of sensory and motor block in brachial plexeus block. Also total duration of analgesia and motor blockade is prolonged when dexmedetomidine is added to bupivacaine and the requirement for analgesic drugs in the postoperative period too is decreased.

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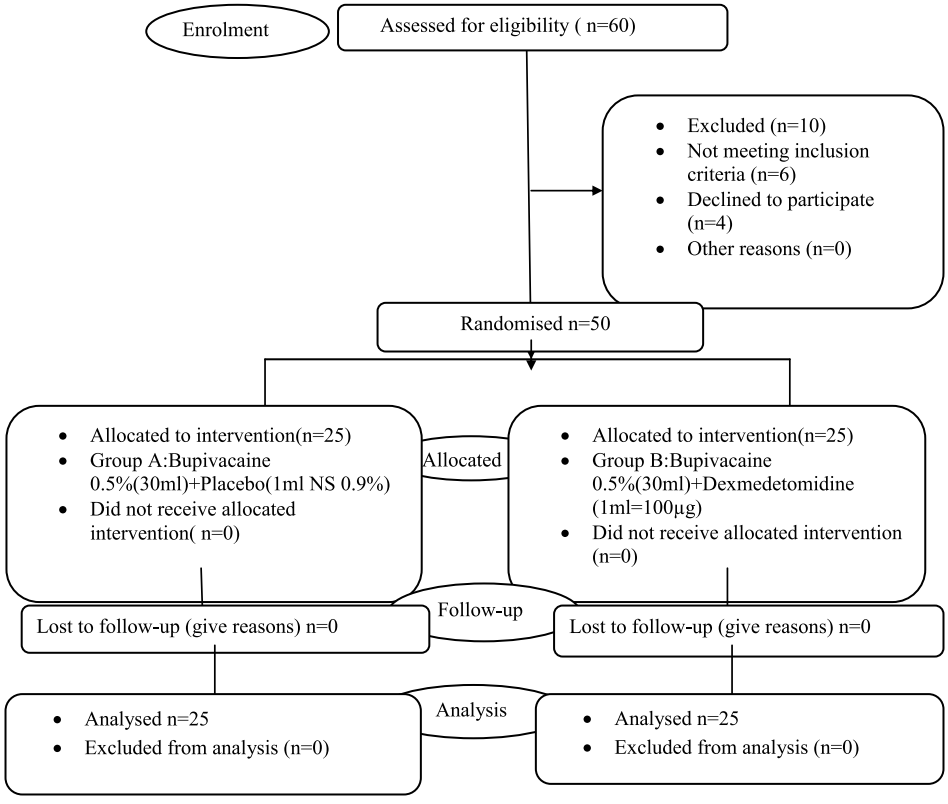

Diagram: Consort flow chart

PARAMETERS	GROUP A	GROUP B	P VALUE
Age(yrs)	32.9+16.1	33.5+13.7	NS
Weight(Kg)	64.4+6.84	64.16+5.9	NS
Gender(M/F)	17/8	15/10	NS
Type of surgeries			
# Radius ulna	12	13	
# Olecranon	10	8	
#Lower end humerus	3	4	

Table 1: Patient's demographic parameters

	GROUP A Mean+SD	GROUP B Mean+SD	P Value
Sensory onset time (min)	10.4+3.57	5.76+2.47	<0.0001
Motor onset time (min)	17+4.8	11.2+3.81	<0.0001
Sensory duration (min)	525+125	713+104	<0.0001
Motor duration (min)	470+123	669.4+105.3	<0.0001

Table 2: Comparison of sensory and motor onset time and duration in both the groups

Time	GROUP A Mean±SD (Pain Score)	GROUP B Mean±SD (Pain Score)	P Value
30 min	0	0	0
2 hr	3.2±5.65	0	0.0067
8 hr	45.6±15.02	5.2±11.59	<0.0001

Table 3: Comparison of Pain scores in both the groups

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Airway Management: Evolving views

Rashid M Khan, Abdullah Al-Jadidi

Concept of airway management has been evolving since the ancient times ranging from the description of mouth to mouth breathing in the bible[1] to robotic airway management in recent times.[2] Between these two extremes, subtle changes were slowly evolving. However lately, a number of well established practices involving the four pillars of routine airway management (mask ventilation, supraglottic airway device placement, tracheal intubation and surgical airway) are being questioned and newer concepts being put forwards.

Time has come for us to review which advances in airway management have an impact on patient safety and needs to be implemented. Given concrete evidence, we should be amenable to changes in the patient's interest.

First pillar of airway management is usually the mask ventilation. It has been the traditional teaching that one should ascertain ease of mask ventilation after induction with intravenous or inhalation induction agents prior to giving muscle relaxant. In case mask ventilation is difficult, teaching was to avoid giving muscle relaxant. This practice is slowly dying. Multiple studies including those of Warters et al in 2011[3] have shown that administration of muscle relaxants most often improves mask ventilation and never shown to deteriorate it. Administration of muscle relaxant offers a second advantage- it permits placement of supraglottic device (SGD) and making hands-free ventilation easier.

Another piece of sound advice given during airway management training was to awaken the patient if difficulty was encountered with mask ventilation. This practice is also being questioned. Today, more and more anesthesiologists are willing to administer muscle relaxant and deepen anesthesia in times of airway difficulty that is more likely to improve mask ventilation, make it easier for placing an SGD or intubate the patient. Using muscle relaxant in patients with difficult airway is now considered very low risk in the hands of skilled airway managers.[4]

During today's general anesthesia, the second airway pillar is often placing a SGD. Laryngeal mask airway (LMA) has brought about a revolutionary change in our airway practice.[5] A mandatory requirement till lately has been a deep level of anesthesia with or without muscle relaxant

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or an absent gag reflex prior to using this invaluable device. Rules are being re-written to the use of SGD in today's practice.

Darren Braude, a well-acknowledged airway educator, coined the term "rapid sequence airway".[6] Generally, we induce the patient with an intravenous induction agent (usually propofol), narcotic (often fentanyl), with or without a non-depolarizing muscle relaxant and then gently assist the patient's breathing for 2-3 minutes before attempting tracheal intubation. In rapid sequence airway, a SGD is placed immediately after administration of induction agents without waiting for full paralysis. This has been shown to ease ventilation till onset of complete paralysis when SGD is removed and tracheal intubation accomplished while others have used the SGD as a conduit for tracheal intubation using an endoscope and an Aintree catheter. Today, tracheal intubation through the SGD aided by flexible endoscopy is widely done in anesthetic practice.[4]

The third pillar of airway management is often considered to be the tracheal intubation. Apneic tracheal intubation following muscle relaxants has traditionally been attempted after a good preoxygenation. Today, the teaching has become to follow NO DESAT (nasal oxygen during efforts securing a tube) policy during difficult tracheal intubation.[7,8] This policy is a result of our understanding that in normal circumstances with apneic oxygenation, a PaO2 can be maintained at >100 mmHg for up to 100 minutes without a single breath, although lack of ventilation shall result in hypercapnia and acidosis.[9] It has been demonstrated in most patients (except those with significant shunting and high positive end-expiratory pressure requirements), that administering oxygen via the nose dramatically prolongs safe apnea period, allowing intubation efforts through the mouth without desaturation. This policy has now been adopted by several airway guidelines.[10, 11] Of course, NO DESAT policy should not deter us from performing 3 minutes of preoxygenation until the end-tidal oxygen fraction is 0.87–0.9 to denitrogenate the lung and build a reservoir of oxygen.

Yet another notable change in our tracheal intubation practice has been the incorporation of video laryngoscopy during airway management. Several well-designed studies have now confirmed that video laryngoscopy results in reduced number of intubation attempts and a better overall intubation success rate, both in routine and difficult airway scenarios.[12-15] It is time that conventional rigid laryngoscopy gives way to videolaryngoscopy in our daily airway management practice. However, fallout of increasing use of videolaryngoscopy has been our declining expertise with fiberoptic tracheal intubation.

In situations where the above three airway techniques do not result in ventilation and/ or oxygenation (eg, distorted anatomy, perilaryngeal or other pathology), sometimes the best option remains in creating a quick surgical airway. Unfortunately, this decision is often the hardest to make during difficult airway management, a decision that makes a difference in patient outcome. The Fourth National Audit Project has highlighted that the success level of surgical airway in times of crisis is just 36%.16 Because this is a core skill for the management of the 'cannot ventilate, cannot intubate' situation, this finding is a serious cause for concern. The solution to this airway lacuna should start from residency training, initial certification exams, and maintenance of certification in anesthesiology to train and assess crisis management especially in undertaking a surgical airway in a timely and successful manner.

Lastly, one of the pillars of safe airway management practice had been application of cricoid pressure during tracheal intubation especially in patients with doubtful gastric

contents or integrity. This seems to be fading into medical oblivion. This has been attributed to the fact that cricoid pressure has been shown to distort laryngoscopic view, occasionally worsen ventilation, and does not reliably prevent regurgitation.[17, 18] In addition, it hampers LMA placement in the upper esophagus, and if applied after LMA insertion, it is observed to push the LMA out of position. The recent Advance Cardiac Life Support guideline no longer recommends its use during CPR.

As of today, cricoid pressure which was considered an essential aspect of rapid sequence tracheal intubation, has come under increasing scrutiny within anesthesia and emergency medicine fraternity and needs an urgent answer to its applicability in airway practice.[19,20].

Present day clinical trials have found many of our current airway practices that need change. We should adopt practices that have withstood test of rigorous trials and have been judged to enhance patient's safety. On the other hand, we should no longer remain tied to airway traditions that have been proven to be harmful or of little value.

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Comparison of Fentanyl with Dexmedetomidine for Smooth Extubation: A Clinical Study

Vibhor Rai, Akhilesh Mishra

INTRODUCTION

Many theories have been described for sudden exaggerated haemodynamic response during intubation and extubation such as release of catecholamines,[1] Extubation can be associated with detrimental airway and hemodynamic responses. Easy extubation requires the absence of straining, movement, coughing, breath holding and laryngospasm.[2] airway irritation, intense pain following surgery, and emergence. other drugs are used to attenuate the intubation response such as intravenous lignocaine,[3] opioids such as fentanyl and remifentanil[4,5] esmolol,[6] labetalol,[7] intratracheal local anaesthetic instillation[8] dexmedetomidine[9] which can be used during extubation also. Many researches has been done to attenuate hemodynamic responses to intubation, but the same care and precautions are seldom carried out for extubation. The aim of this study was to compare the effect of sedation with single-dose dexmedetomidine and fentanyl on the attenuation of circulatory and airway response to endotracheal extubation.

METHODOLOGY

After Institutional Ethical Committee approval and written informed consent from patients, this double-blind, randomized, prospective clinical trial was carried out over a period of 6 months on fifty patients of American Society of Anesthesiologists (ASA) Grades 1 and 2 of both male & female sex , aged above 18 years undergoing surgery under general anesthesia. Patients randomization were done into two groups by sealed envelope technique; Group D received dexmedetomidine 0.7 µg/kg and Group F received fentanyl 1 µg/kg. Patients with upper respiratory tract infection and those required intra-operative nasogastric tube were excluded from the study.

All patients were premedicated with oral alprazolam 25 mcg in the night and tablet ranitidine 150 mg in the morning of the surgery. On the operating room table, after securing an intravenous access, injection midazolam 1.5 mg and injection ondansetron 4 mg were given. Base

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line hemodynamic parameters such as HR, BP, oxygen saturation were recorded with a multiparameter monitor. All participants were anesthetised using standard anesthesia technique. All patients were induced with propofol 2 mg/kg, morphine 0.1 mg/kg. Tracheal intubation was done using vecuronium (loading dose of 0.1 mg/kg, intermittent bolus of 0.02 mg/kg) and anesthesia was maintained on O2:N2O (0.5 L: 0.5 L) and isoflurane 2 % dial concentration adjusted to maintain minimum alveolar concentration to 1. An additional dose of morphine was given depending on hemodynamics. Isoflurane stopped fifteen minutes before expected last surgical suture, isoflurane was stopped, and equal amount of test solution (10 ml) was given over a period of 5 min by infusion pump. The test solution was prepared by anesthesiologist who was not involved in the study. Five minutes after the infusion, the patient was reversed from muscle relaxant effect with injection neostigmine 50 µg/kg and glycopyrrolate 10 µg/kg. Hemodynamics was assessed at every 2 minutes for first 10 minutes then every 5 min interval from the time of study drug administration up to 15 min after extubation. The level of sedation during suction and extubation was assessed using ramsay sedation scale (Table 1). The level of sedation during suction was assessed, and airway response under direct laryngoscopy to suction was noted by five-point scale.

(Table 2). After 5 min interval, the level of sedation was assessed, and smoothness of extubation was noted by four-point scale (Table 3]. When mean arterial BP fall more than 10% of baseline value, 150 ml fluid bolus was given, and injection mephentermine was supplemented intravenously if there was no improvement. Drop in HR more than 20% from baseline was treated with injection atropine 0.6 mg intravenously.

Table 1

Observer assessment sedation score

OBSERVATION	SCORE
Responds readily to name spoken in normal tone	5
Lethargic response to name spoken in normal tone	4
Reponds only after name is called loudly/ repeatedly	3
Responds only after mild prodding or shaking	2
Does not respond to mild prodding or shaking	1

Table 2

Grading of airway reflexes

Grade	Description
1	Excellent (breathing well, no response to laryngoscopy, and suctioning)
2	Good (breathing well, minimal grimacing response to laryngoscopy and suction
3	Satisfactory (breathing well, coughing attempt to laryngoscopy and suction)
4	Poor (breathing well, coughing on tube during laryngoscopy)
5	Very poor (coughing on tube with breath holding)

Table 3

Smoothness of extubation

Grade	Description
1	No coughing on endotracheal tube
2	Coughing on tube
3	Vomiting
4	Laryngospasm

Statistical analysis

Based on our study, 13% difference in HR and BP between baseline and extubation between two groups was observed. For α 0.06 and β 75%, 23 patients per treatment group were needed. Assuming a 7% dropout rate, fifty patients (25 patients per group) were recruited for the study.

Data Statistical analysis is done using Statistical Package for Social Sciences (SPSS Version 19, IBM Corporation, Armonk, North Castle, New York, United States). Statistical analysis was done using paired-samples t-test for between group comparisons. The Chi-square test was used to analyze extubation quality, sedation scores, and adverse events. $P < 0.05$ was considered as statistically significant.

RESULTS

Age, weight, gender, airway, and ASA physical status were comparable in both groups. The total dose of morphine consumed by the patients was not statistically significant [Table 4].

Table 4

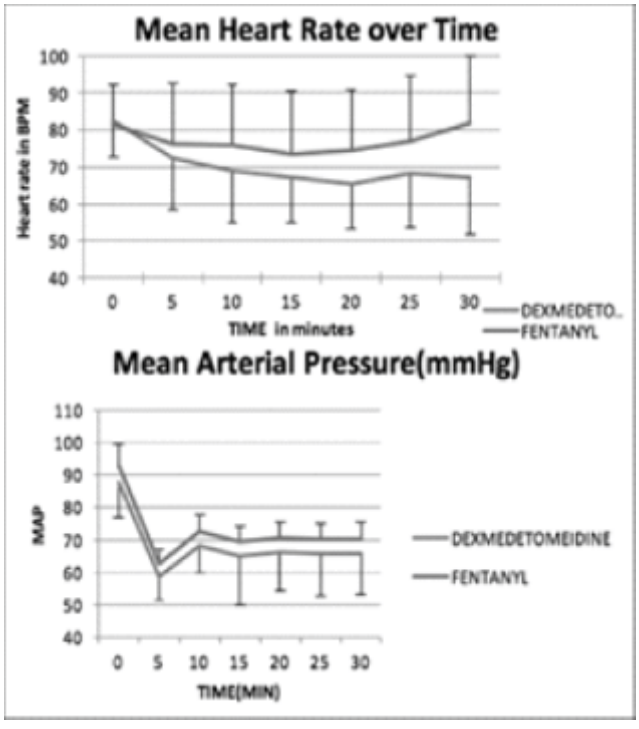
Demographic data and total morphine consumption

Parameters	Dexmedetomidine	fentanyl	P
Age-mean (95% CI)	34.86 (30.27- 42.88)	38.24 (33.07-43)	0.356
Gender (male:female)	13:12	8:15	0.136
MPC* (1/2)	11/14	8:17	0.144
ASA* (1/2)	19/2	19/2	1.2
Weight-mean (95% CI)	57.64 (51.46-59.33)	61.84 (57.34-66.02)	0.156
Morphine consumption Mean (95% CI)	6.54 (6.21-7.8)	6.73 (6.31- 7.44)	0.811

*Mallampatti class, *American Society of Anaesthesiologist, CI= Confidence interval

Decrease in HR shown in both the groups , from the time of test drug administration to extubation. However, dexmedetomidine produced a significant drop in HR when compared to fentanyl. Increase in HR in fentanyl group seen post extubation [Figure 1].

Figure 1 : Hemodynamic variations over time



Reduction in BP was observed in both groups at 5 min post drug administration, which improved with fluid bolus and was maintained within 10% of baseline value throughout. [Figure 1].

Dexmedetomidine group patients showed greater degree of sedation during suctioning of airway and extubation when compared to fentanyl. Dexmedetomidine group patients was arousable but not awake post extubation but fentanyl group patients was awake. That is the reason that there HR was increased post extubation [Figures [Figures 22 and 33].

Figure 2 : Level of sedation and grading of smoothness during extubation

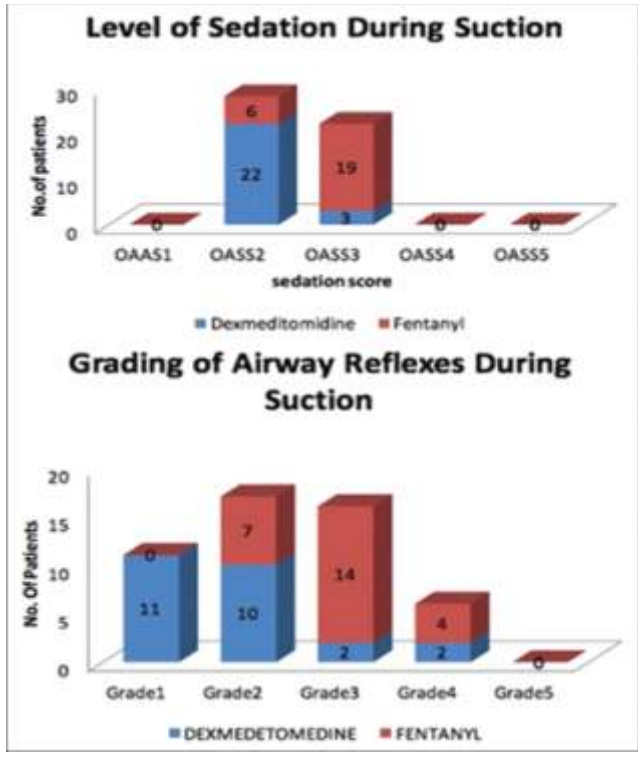


Figure 3 : Level of sedation and grading of airway reflexes during suction

Dexmedetomidine group patients in larger number tolerated laryngoscopy and suction. In both groups, none of the patients had breath holding or difficulty in tolerating the endotracheal tube [Figure 3].

DISCUSSION

Recouping from anesthesia regularly brings about hoisted haemodynamic parameters because of catecholamine focus following soporific withdrawal which is additionally irritated by laryngeal control happening amid extubation. Dexmedetomidine, a strong alpha-adrenoceptor agonist, diminish the thoughtful surge and noradrenergic movement accordingly neutralizing the hemodynamic variance happening at the time of extubation9 and fentanyl is a demonstrated medication to lessen the intubation and extubation reaction. We analyzed the impacts of dexmedetomidine and fentanyl in constriction of hemodynamic and airway reflexes amid rise and extubation.

Dexmedetomidine initiates receptors in the medullary vasomotor focus, lessening norepinephrine turnover and diminishing central sympathetic outflow, resulting in alterations in sympathetic function and decreased HR, and BP. In our study, patients of both groups showed drop in HR and BP all through the examination time frame. On correlation between the groups, dexmedetomidine assemble demonstrated a critical drop in BP at 5 min interim after medication organization and enhanced with liquid boluses. Kothari et al.[10] looked at lignocaine and dexmedetomidine and watched that solitary measurements of dexmedetomidine 0.5 μg/kg given 5 min before extubation delivered better weakening of hemodynamic reaction in craniotomy patients. Nonetheless, Sharma et al.[11] found an expansion in mean arterial pressure for initial 3 min in dexmedetomidine group which might be because of bolus medicate organization impact and diminished from standard incentive after 5 min.

Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus ceruleous in the brainstem plays a prominent role in the sedation and anxiolysis produced by dexmedetomidine. There was increase in HR and BP in fentanyl group after extubation when compared to dexmedetomidine group which could be attributed to good sedation score provided by dexmedetomidine than fentanyl. Aksu et al.[12] also found similar hemodynamic response of increase in HR and BP after the extubation of rhinoplasty patients in fentanyl group when compared with 0.5 μg/kg dexmedetomidine.

Kim and Bishop [13] discovered 76% occurrence of coughing during emergence. coughing can bring about hypertension, tachycardia, increases intraocular and intracranial tension, myocardial ischemia, bronchospasm, and surgical bleeding.[14] In our investigation, dexmedetomidine group demonstrated better airway response during laryngoscopy and oral suctioning when contrasted with fentanyl which connected well with better sedation score in dexmedetomidine group. The smoothness of extubation was equivalent between the two groups. Guler et al. watched that solitary dosage of dexmedetomidine 0.5 μg/kg when given 5 min before extubation encouraged resilience of endotracheal tube and altogether diminished coughing during extubation without influencing the development time.[15]

Fan et al. did a comparative report contrasting remifentanil and two measurements of dexmedetomidine 0.5 μg/kg and 0.7 μg/kg for otology surgery and watched that higher rate of patients in dexmedetomidine groups had smooth extubation in regards to the nonappearance of bucking and coughing during head surgical dressing.[16] They likewise watched that occurrence of postoperative nausea and vomiting was less with dexmedetomidine group.

To rule out the morphine enhancing the sedation effects during extubation, we observed total morphine consumption during the intra-operative period in both the groups and found to be comparable between the two groups.

Aside from measurably huge drop in BP at 5 min of medication organization which reacted to liquid bolus in the dexmedetomidine assemble there were no unfriendly symptoms amid the examination time frame. Both groups had a similar duration of recovery from anesthesia without delay in emergence. Dexmedetomidine 0.75 μg/kg given over 15 min before extubation enabled smooth extubation of the trachea and provided adequate sedation postoperatively with increase in the incidence of bradycardia and hypotension.[17]

Limitations

We examined the single dosage of dexmedetomidine and fentanyl for attenuation of hemodynamic and airway reflexes. A dose

response study might be valuable in deciding the suitable dosage of the examination drugs. Second, five guide airway reaction toward suction under direct laryngoscopy and airway reaction to extubation have not been approved.

CONCLUSION

Single-dosage dexmedetomidine 0.75 μg/kg given 15 min before extubation created better attenuation of airway reaction to laryngoscopy and airway suctioning. This resulted in smooth tracheal extubation without prolonging recovery when compared to fentanyl.

SUMMARY

This double-blind, randomized, controlled study was done in patients undergoing surgery under general anesthesia belonging to (ASA) physical status 1 or 2 to compare the effects of fentanyl 1 μg/kg and dexmedetomidine 0.75 μg/kg in attenuating airway and circulatory reflexes during emergence and extubation of the endotracheal tube. Study drug was given 15 min before the end of surgery as an infusion and over 15 min post extubation. Hemodynamic parameters and patient response for laryngoscopy and oral suctioning and during extubation were graded. Dexmedetomidine was found to produce hypotension at 5 min of drug infusion and improved with fluid bolus; HR was stable throughout the study period. Extubation quality was found to be superior in dexmedetomidine group with patients arousable and tolerating suctioning and extubation. Whereas in fentanyl group, patients were awake during extubation and had tachycardia after extubation.

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Evaluation of the efficacy of different concentrations of levobupivacaine with dexmedetomidine for ultrasound guided supraclavicular brachial plexus block.

Farah Nasreen,[1] Shoaib Parvez,[2] Hammad Usmani,[3] Nazia Tauheed[4]

ABSTRACT

Background: Supraclavicular brachial plexus block is a routinely performed technique for surgeries of arm and forearm. Decreasing the concentration of local anaesthetic drug without compromising block characteristics increases the margin of safety of brachial plexus block. In this randomized double blind study, we evaluated the efficacy of two different concentrations of levobupivacaine viz 0.375% and 0.25% with dexmedetomidine for ultrasound guided supraclavicular brachial plexus block (SBPB).

Material and Methods: Sixty ASA Grade I and II patients in the age group of 18-60 years scheduled for upper limb surgery, were randomly divided into two groups: Group I received SBPB with 30 ml levobupivacaine 0.375% with dexmedetomidine 1µg/kg. Group II received SBPB with 30 ml Levobupivacaine 0.25% with dexmedetomidine 1µg/kg. Onset and duration of sensory and motor blockade, duration of analgesia, patient satisfaction score, and hemodynamic parameters were observed in both the groups.

Results

Onset of sensory and motor blockade was 13.3 ±1.97 mins and 16 ±3.2 mins in group I, while it was 17.8±2.34 mins and 22.8±1.92 mins in group II, respectively. The difference was statistically significant ($P < 0.05$). The duration of motor block was significantly lesser in group II (819 ± 109.6 mins) as compared to group I (1207±110 mins). The requirement of rescue analgesics between the two groups was comparable during first 24 hrs (p value >0.05). Group II patients had significantly better patient satisfaction score than group I patient

Conclusion

Both the concentrations of levobupivacaine with dexmedetomidine can be effectively used for ultrasound guided supraclavicular brachial plexus. Although, the onset time of sensory and motor blockade is significantly reduced using a higher concentration of levobupivacaine i.e. 0.375%, there is early return of motor functions and subsequently better patient satisfaction with 0.25% levobupivacaine.

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Key words
Levobupivacaine, Dexmedetomidine, supraclavicular brachial plexus block.

Introduction

Supraclavicular brachial plexus block has been widely used for surgeries including arm, forearm and hand. Although bupivacaine is one of the most commonly used local anaesthetic for central and peripheral nerve blocks, the potential for cardiotoxicity has led to the development of interest in levobupivacaine, a safer alternative in this respect[1,2]. In brachial plexus blocks where larger doses of local anaesthetics are administered, levobupivacaine is preferred due to greater margin of safety.[3]

Use of ultrasound in brachial plexus block has revolutionized the technique as direct visualisation of nerve structures and real time control of local anaesthetic administration leads to reduction in overall volume of anaesthetics and consequent overdose risk. [4,5]

Addition of adjuvants to local anaesthetic in brachial plexus block increases its efficacy. The ability of dexmedetomidine to reduce the requirement of local anaesthetic and analgesics is increasingly being used in perioperative period. When combined with local anaesthetic for brachial plexus block, dexmedetomidine has been found to effectively reduce the concentration required for the block along with the improved block characteristics.[6–8] Studies have shown that addition of dexmedetomidine lowers the concentration of local anaesthetic for supraclavicular brachial plexus block[9-10]. However, there is relative scarcity of literature on the use of dexmedetomidine as adjuvant to lower concentrations of levobupivacaine in supraclavicular brachial plexus block.

The present study was thus designed to compare the efficacy of 0.25% levobupivacaine with dexmedetomidine to 0.375% levobupivacaine with dexmedetomidine under ultrasound guidance for supraclavicular brachial plexus block in terms block characteristics, overall patient satisfaction score and side effects.

Material and Methods

Following approval by the Board of Studies, Department of Anesthesiology, and Institutional Ethics committee, the study was conducted in the Department of Anesthesiology, J N Medical College and Hospital AMU Aligarh. Sixty patients, ASA Physical Status I and II aged between 18–60 years, weight 40-70 kg, undergoing upper limb surgery were included in this prospective randomized double blind study after a written informed consent.

Patients with severe cardiorespiratory, renal or hepatic disease; pregnancy; patients with peripheral neuropathy; coagulopathy; infection at the site of block and patients with known allergy to local anesthetic were excluded. The patients were randomly allocated to two groups of 30 each and brachial plexus block was performed under ultrasound guidance, in-plane technique.

Group I received 30 ml of Levobupivacaine 0.375% with dexmedetomidine at dose of 1 µg/kg of body weight and Group II received 30 ml of Levobupivacaine 0.25% with dexmedetomidine at dose of 1 µg/kg of body weight. Drug was prepared beforehand by personnel not involved in the study and handed over to the team performing the block.

Baseline heart rate, blood pressure, and oxygen saturation were recorded. An intravenous line with 18-gauge intravenous cannula secured in the unaffected limb and Ringer's Lactate infusion was started.

Sensory block was assessed by blunt tip needle test over C5-T1 dermatomes and graded as: Grade 0: sharp pain felt, Grade 1: dull pain felt, Grade 2: no pain felt. Motor block assessment

was done and graded on a four-point scale; i.e. Grade 0: Full flexion /extension movement in hand and arm against resistance, Grade 1 – movement against gravity but not against resistance, Grade 2 – flicker of movement in hand but not in arm, Grade 3 – no movement (complete motor block).
All patients in each group were independently observed for:

A) Onset time of sensory block; Time interval between end of local anaesthetic administration and complete loss of pain sensation (Grade 2) B) Duration of analgesia; Time from administration of drug to appearance of pain, requiring analgesic (NRS >3)*. Pain was assessed on a rating scale, zero representing no pain and 10 meaning worst possible pain. Injection tramadol 2mg/kg intravenous infusion was given as rescue analgesic when the pain score was more than 3. C) Onset time of motor block was defined as a time interval between end of local anaesthetic administration and appearance of motor block Grade 2. D) Duration of motor block; Time interval from complete motor block to recovery of complete motor function of hand and forearm (Grade 0) E) Overall satisfaction of patient was evaluated 24 hours after surgery using five point satisfaction scale; 1 = very dissatisfied, 2 = dissatisfied, 3 = uncertain, 4 = satisfied, 5 = very satisfied F) Heart rate, non-invasive blood pressure and oxygen saturation were measured immediately after administration of drug, 5 min,10 min,20 min,30 min and then at intervals of every fifteen minutes till the completion of the operation.

G) Complication or side effects as a result of the procedure such as bradycardia (HR<50 bpm), hypotension (decrease in baseline BP by >20 %), hypertension (rise in baseline BP >20 %) nausea, vomiting, and hypoxemia (SpO2 <90%) convulsions, pneumothorax, pleuritis, jerky movements, Horner's syndrome, hypersensitivity reaction.

Statistical analysis

Statistical analysis performed done using Graph Prism Pad Software Inc. Parametric data(age, weight, timings) were analyzed using Unpaired t test. Non parametric data were analyzed using the Fisher's exact test.

Results

In the present study, 60 patients were divided into two groups of 30 each, group I receiving 0.375 % levobupivacaine with dexmedetomidine (1µg/kg body weight) and group II receiving 0.25 % levobupivacaine with dexmedetomidine (1 µg/kg body weight), {total volume of drug was diluted to 30 ml}.

The two study groups were similar in terms of their demographic profile (table 1). The minor differences observed were statistically insignificant (p value >0.05). The mean onset time of sensory block in group I was 13.3 ± 1.97 mins whereas it was 17.8 ± 2.34 mins in group II (table 2, figure 1). The difference was statistically significant (p value <0.05). The mean onset time of motor block in group I was 16 ± 3.2 mins and in group II, it was 22.8 ± 1.92 mins (table 2, figure 2). On comparison, the difference was statistically significant (p value <0.05). The difference between the two study groups in terms of duration of analgesia (table 2) was not statistically significant (p value >0.05). The duration of motor block was significantly lesser in group II(819 ± 109.6 mins) as compared to group I(1207±110 mins) [table 2 , figure 3]. The requirement of rescue analgesics between the two groups was comparable during first 24 hrs (p value >0.05) [table2]. Group II patients had significantly better patient satisfaction score than group I patient (p value<0.05)[table 3]. The baseline haemodynamic parameters, pulse rate, blood pressure, SpO2 variation during and after block was seen to be similar in both the study groups with no statistically significant difference. One patient in group I had vomiting, two patients in

both the groups were sedated intraoperatively and two hours postoperatively but there was no sign of respiratory depression. None of the patients in group I and group II had other complications like bradycardia and hypotension.

Table 1: Demographic profile

Parameter	group I (n=30)	group II (n=30)	p value
age (years)	32±16	33±13	0.88
weight (kg)	60±9.78	60.3±6.16	0.894
Male : Female	21:9	19:11	0.7487

Table 2: Block characteristics

Table 2: The characteristics of block			
	Group 1 (n = 30) Mean ± SD	Group II(n = 30) Mean ± SD	P value
Onset time of sensory block(mins)	13.3 ± 1.97	17.8 ± 2.34	<0.0001
Onset time of motor block(mins)	16 ± 3.2	22.8 ± 1.92	<0.0001
Duration of analgesia (mins)	851 ± 139	789 ± 108	> 0.05
Duration of motor block (mins)	1207 ± 200	819 ± 109.6	<0.0001
Total number of rescue analgesics	2±0.60	2.2±0.47	>0.05

Figure 1: Onset time of sensory block in study groups

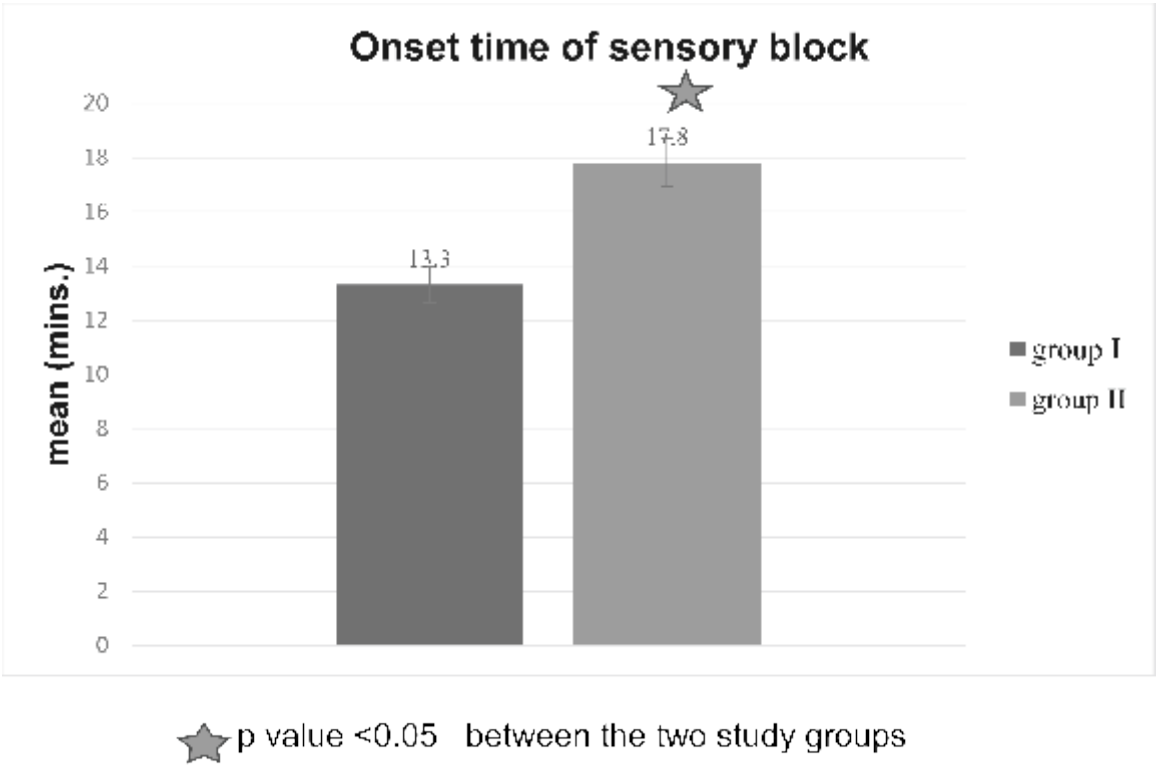

Figure 2: Onset time of motor block

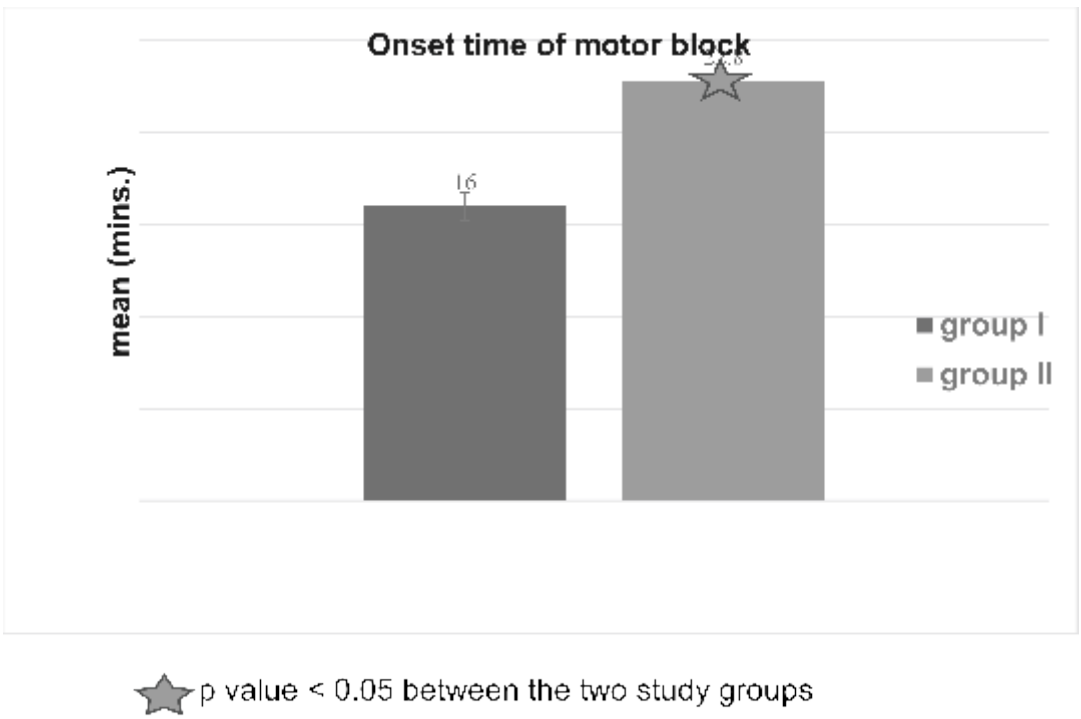

Figure 3: Mean duration of motor block

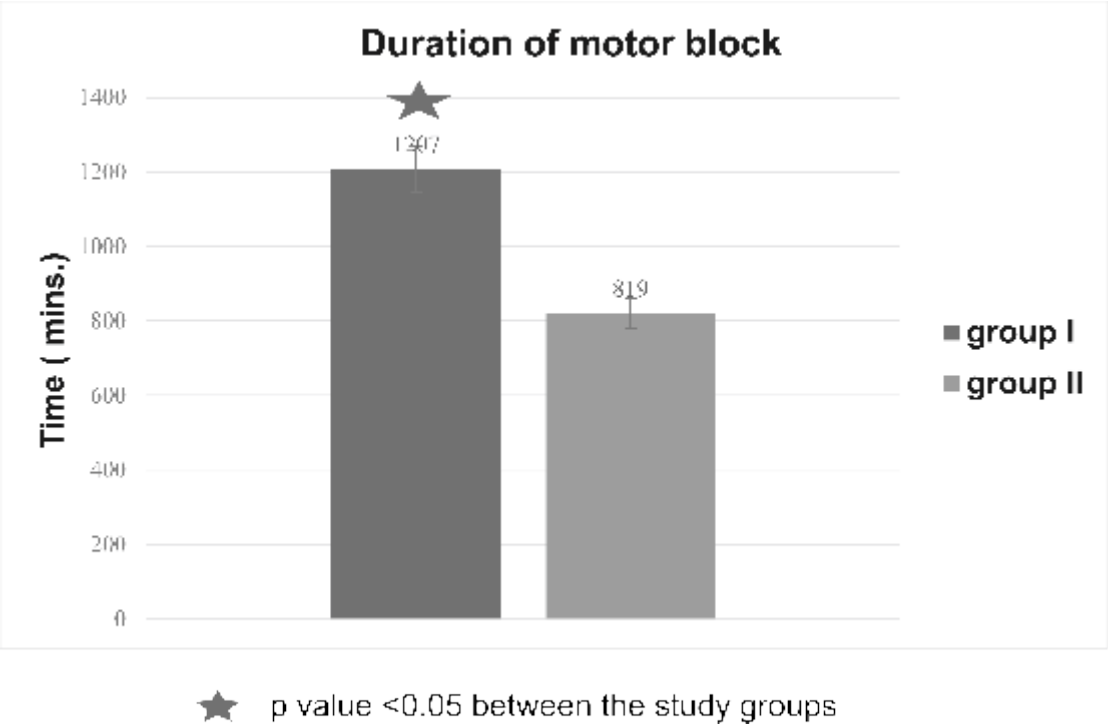

Table 3: Comparison of patient satisfaction score between study groups

	group I	group II	P value
Mean	3.96	4.83	<0.0001
SD	0.65	0.37	

Discussion

In this randomised double-blind study, two different concentrations of levobupivacaine with dexmedetomidine were compared for ultrasound guided supraclavicular brachial plexus block. It was observed that the mean onset time for sensory and motor blockade was shorter with a higher concentration of levobupivacaine (0.375%) with dexmedetomidine as compared to the lower concentration (0.25%). The duration of analgesia was however, comparable in both the groups. The duration of motor block was less with the lower concentration of levobupivacaine (0.25%), which might have led to an overall better patient satisfaction score.

In brachial plexus block, where large doses of local anaesthetics are used, reduction in total dose of local anaesthetic has advantage of reducing the risk of local anaesthetic toxicity. Secondly with the lower doses, there is early return of motor activity and better patient satisfaction score.

Baskan et al[11] compared the onset time and quality of posterior approach interscalene brachial

plexus block produced by 0.25% levobupivacaine and 0.25% bupivacaine and proved the efficacy of 0.25% levobupivacaine in posterior approach interscalene brachial plexus block. They observed similar motor and sensory block onset times and qualities and concluded that both drugs provide an equally comfortable anaesthesia and analgesia for shoulder surgery.

Cox et al[12] compared bupivacaine and levobupivacaine in brachial plexus block. They observed that 0.25% levobupivacaine had slower onset and shorter duration of action and lower overall success rate compared to 0.5% levobupivacaine, although this difference was not found to be statistically significant. The present study also shows a slower onset and shorter duration of action with 0.25% levobupivacaine. The overall patient satisfaction was, however found to be better with this concentration and a statistically significant difference was found.

Role of dexmedetomidine as adjuvant to local anaesthetics in brachial plexus block has been validated in several studies.[9,13-15] Studies have shown that addition of dexmedetomidine lowers the concentration of local anaesthetic for supraclavicular brachial plexus block.[9,10] The ability of dexmedetomidine to reduce the requirement of local anaesthetic and analgesics has been increasingly used in the perioperative period.

Addition of dexmedetomidine to local anaesthetic in brachial blocks significantly prolonged the duration of analgesia and motor blockade. Dexmedetomidine in clinically effective doses lacks respiratory depression[16,17] but maintains its analgesic properties that may make it useful and safe adjunct in many diverse clinical applications.

An early onset of sensory block with higher concentration of levobupivacaine was seen in this study, keeping the dose of dexmedetomidine constant in both the groups.

Kim et al[18] compared 0.375% levobupivacaine with 0.5% levobupivacaine for ultrasound guided axillary brachial plexus block and showed equivocal results without clinically significant difference compared to 0.5% levobupivacaine. They have demonstrated the average elapsed time to be ready for surgery was 26 mins, whereas, in this study the onset of motor block with 0.375% levobupivacaine was 16 mins. This shorter onset time of motor block could be attributed to the addition of dexmedetomidine with local anaesthetic drug.

Effect of addition of dexmedetomidine(100 µg) to levobupivacaine (0.5%) was studied by Esmaoglu et al[19] for axillary brachial plexus block. They concluded that addition of dexmedetomidine shortens the onset time of both sensory and motor block. A similar study by Kaygusuz et al[20] also demonstrated a short sensory block onset time with the addition of dexmedetomidine(1µg/kg).

Patients in both the groups achieved adequate duration of surgical analgesia during the perioperative period. Although the duration of analgesia was longer with 0.375% levobupivacaine than 0.25% levobupivacaine, the difference was statistically insignificant.

However, such findings were in contrast to the study of Hickey et al [21] who demonstrated that 0.25% concentration of levobupivacaine for brachial plexus is not sufficient to achieve surgical anaesthesia because of slow onset and a high rate of inadequate block.

The addition of dexmedetomidine with 0.25% levobupivacaine could have led to the enhanced analgesic efficacy of supraclavicular brachial plexus block in this study.

Palsule et al[9] conducted a study to evaluate the effect of dexmedetomidine as an adjuvant to 0.25% bupivacaine in supraclavicular block (SCB) and concluded that adding dexmedetomidine

(1µg/kg) to bupivacaine (0.25%) during supraclavicular BPB shortens sensory and motor block onset time, increases the sensory and motor block duration, and prolongs the duration of postoperative analgesia without any significant side effect.

Biswas et al[22] evaluated the effect of combining dexmedetomidine with levobupivacine with respect to duration of motor and sensory block and duration of analgesia and demonstrated that addition of dexmedetomidine to levobupivacaine 0.5% prolongs the duration of motor and sensory block and extends the duration of analgesia.

Nallam et al[23] conducted a study to evaluate the effect of adding different doses dexmedetomidine (50 µ g and 100 µg) to 0.5% levobupivacaine and found a significantly prolonged duration of analgesia with the higher dose.

Other studies have also demonstrated that the duration of sensory and motor blockade could be prolonged with dexmedetomidine as adjuvant to levobupivacaine in brachial plexus block.21,24,28 Williams et al[24] conducted a prospective study to assess the quality, safety, and execution time of supraclavicular block of the brachial plexus using ultrasonic guidance and neurostimulation in comparison with a supraclavicular technique that used anatomical landmarks and neurostimulation. Authors found that ultrasound guidance allowed statistically and clinically significant reductions in procedure times and provided better block quality than a neurostimulator-guided subclavian perivascular approach.

Kaygusuz et al20 have also shown that adding dexmedetomidine to levobupivacaine in axillary BPB increases the sensory and motor block duration and time to first analgesic use, and decreases total analgesic use with no side effects. The prolongation of duration of sensory and motor block with dexmedetomidine as an adjuvant to bupivacaine in brachial plexus block was also confirmed by Gandhi et al.[25]

In another study, Haramritpal et al[26] evaluated the effect of addition of dexmedetomidine to varying concentrations of levobupivacaine (0.5% and 0.25% levobupivacaine) for supra clavicular brachial plexus block. In this study, they demonstrated that the addition of dexmedetomidine to levobupivacaine can significantly decrease the concentration of levobupivacaine required for surgical anaesthesia, shortens the sensory and motor block onset time, reduces the offset time for motor block, prolongs the duration of postoperative analgesia and provides comparable overall satisfaction scores among patients. Reduction in total levobupivacaine dose also increases the safety margin of the block.

In this study, the duration of motor block was significantly shorter with 0.25% levobupivacaine [819 minutes] as compared to 0.375% [1207 minutes]. Reduction in the concentration of levobupivacaine from 0.375% to 0.25% might have led to early return of motor function.

The present study also shows a trend towards better satisfaction score with lower concentration of levobupivacaine. The inability to use the affected limb due to prolonged motor block has been shown to reduce patient satisfaction in other studies also.[27,28] Moreover, prolonged motor block hampers the assessment of neurological function after surgical procedures which is not desired by the surgeons.

Dexmedetomidine may lead to side effects such as hypotension and bradycardia with increased dosage along with its effects such as sedation and anxiolysis. In this study, two patients from both the study group remained sedated for two hours postoperatively but arousable without any sign of respiratory depression.

Ultrasound guided technique could have led to better precision and hence we could not find procedure related complications like pneumothorax, Horner's syndrome, vascular punture etc.

One patient in group I had one episode of vomiting. Nausea and vomiting were not seen in group II patients.

There are some limitations to our study. First, it was a monocentric study and small sample size was chosen. Larger randomized controlled trials may be required to validate the findings of our study. Second, follow up period in our study was too short (24 hrs). Long term follow up may be needed to look for neurological complications.

Conclusion

To conclude, the present study suggests that levobupivacaine in concentrations of 0.375% and 0.25% with dexmedetomidine can be effective in producing sensory & motor blockade when administered for supraclavicular brachial plexus block under ultrasound guidance. Although, the onset time of sensory and motor blockade is significantly reduced using a higher concentration of levobupivacaine i.e. 0.375%, there is early return of motor functions and subsequently better patient satisfaction and better assessment of post-surgical recovery of functions with 0.25% levobupivacaine.

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GUIDELINES TO CONTRIBUTORS

Asian Archives of Anaesthesiology and Resuscitation (AAAR) was started in 1971 by initiative of late Prof. W.E. Spoeral of University of Western Ontario, London. He visited JIPMER, Pondicherry in 1970-71 and helped in starting this journal .Since then, AAAR was published under able guidance of (late) Prof. N.P. Singh continuously till date.

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Type or print out the manuscript double spaced, including title page, summary (abstract) and key words, text, acknowledgements, references, tables (each table complete with title and foot notes on a separate page) and legends for illustrations. Each of the above mentioned component of the manuscript should begin with a new page, maintaining the sequence. Illustrations must be of good quality, unmounted glossy prints, usually 1227 x 173 mm (5 x 7 in) but not larger than203 x 254 mm (8 x 10 in). Manuscript should be submitted in CD in Microsoft Word format along with two hard copies (on paper as specified below) with a covering letter, as described under 'Submission of Manuscripts' and permission to reproduce previously published material or to use illustrations that may identify human subjects. From time to time the editor will request for 'Review Articles' on any particular topic. So, review articles may kindly be sent only on such requests. Authors should keep copies of everything submitted.

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Conclusions
Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not completely supported by your data.

Acknowledgements
They should be brief and should include reference to the source of technical help, material support and

financial assistance. Individuals named must approve their inclusion in the acknowledgements, before the paper is submitted.

References

The references of the article are the foundation on which the work of the study is built. They provide the scientific background that justifies your study, including the methods used. AAAR follows 'Vancouver style' of quoting the references as superscripts in which references are numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses. References cited only in tables or in legends to figure should be numbered in accordance with a sequence established by the first identification in the text of the particular table or figure. Use the style of the examples below, which are based with slight modifications on the formats used by the U S National Library of Medicine in Medline database. The titles of journals should be abbreviated according to the style used in Medline. The references must be verified by the authors(s) against the original documents. Restrict references to those that have a direct bearing on the work described, preferably less than 25 for general articles and 6 for short communications.

Examples of correct forms of references are given below.

A. Journals:

1. Standard journal article List all authors, but if number exceeds six, list only first three and add et al. Fery AM, Haynes AR, Owen KJ, Farrall M, Jack LA, Lai LY, et al. Predisposing locus for Alzheimer's disease on chromosome 21, Lancet 1989; 1: 352-5.
2. Organisation as author : The Royal Marsden Hospital Bonemarrow Transplantation Team. Failure of syngeneic bonemarrow graft without preconditioning in post- hepatitis marrow aplasia. Lancet 1977; 2: 742-4.
3. No author given : Coffee drinking and cancer of the pancreas (editorial). BMJ 1981; 283:628. B. Books and other Monographs

1. Personal author(s): Colson JH, Armour WJ. Sports injuries and their treatment, 2nd rev. ed. London: S. Paul, 1986.
2. Editor(s), compiler as authors : Diener HC, Wilkinson M, editors. Drug-induced headache. New York: Springer Verlag, 1988.
3. Chapters in a book: Weinstein L, Swartz MN. Pathologic properties of invading microorganisms. In:Sodeman WA Jr, Sodeman WA, editors. Pathologic physiology: mechanisms of disease. Philadelphia: Saunders, 1974: 457-72.

C. Other published Material

Newspaper article: Rensberger B, Specter B, CFCs may be destroyed by natural process. The Washington Post 1989 Aug. 7; Sect. A:2 (Col.5).

D. Unpublished Material

Lillywhite HD, Donald JA. Pulmonary blood flow regulation in an aquatic snake. Science. In press or Personal Communication

E. Internet References

Complete Website address and the location to be mentioned. Tables Do not include tables in the text. Type each table, double-spaced on a separate sheet.

Number tables consecutively in the order of their first citation in the text and put a brief title for each. Give each table a short abbreviated heading, Mention explanatory matter as well as explanations of all non-standard abbreviations used in the table, in footnotes and not in the heading. Identify statistical measures of variations such as standard deviation and standard error of the mean. Indicate approximate position of each table in relation to the subject matter of the text right hand margin of the appropriate page of the manuscript. If you use data from another published or unpublished source, obtain permission and acknowledge fully. Maximum tables allowed in any manuscript is as follows:

Maximum tables allowance

General Article (excluding abstract)	6
Case Report	2
Brief Report	4
Technical Communication	5
Review Article	10
Medical Intelligence Article	6
Special Article	6
Editorial	1
Letter to the Editor	2

Illustrations (Figures)

Submit two complete sets of figures. Figures should be professionally drawn and photographed; free hand or typewritten lettering is unacceptable. Instead of original drawings, roentgenograms, and other material, send sharp, glossy, black and white photographic prints as mentioned earlier. Letters, numbers, and symbols should be clear and even throughout and of sufficient size that when reduced for publication each item will still be legible. Each figure should have a label pasted on its back indicating the number of the figure, author's name and top of the figure. Do not write on the back of figures or scratch or mark them by using paper clips. Figures should be numbered consecutively according to the order in which they have been first cited in the text. If a figure has been published, acknowledge the original source and submit written permission from the copyright holder to reproduce the material. Do not include these in the text. Indicate the appropriate position of each figure in relation to the subject matter of the text in the right hand margin of the appropriate page of manuscript.

Units of measurement

All measurements – length, height, weight and volume,etc. should be reported in metric units (metre, kilogram, or litre) or their decimal multiples. Temperatures should be given in degree Celsius. Blood pressure should be given in millimetres of mercury. All haematologic and clinical chemistry measurements should be reported in the metric system in terms of the International System of Units (SI).

Abbreviations and Symbols

Use only standard abbreviations. Avoid abbreviations in the title and abstract. The full term for which an abbreviation stands, for should precede its first use in the text unless it is a standard unit of measurement.

Correspondence

A. Letters to the editor include brief constructive comments concerning previously published articles or brief notations of general interest. The manuscripts must be double-spaced, and a title and two copies must be provided. Letters may be submitted at aaarjournal@gmail.com .

B. The editor may change, delete or modify in any way all items of correspondence. Maximum Word Allowance: When submitting your manuscript, please observe the maximum word count allowed for each type of submission; and the maximum allowance for figures, tables, and references (word count should reflect text only and must be listed in the cover letter):

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General Article (excluding abstract)	3000 words
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Brief Report	1000 words
Technical Communication	1500 words
Review Articlc	4000 words
Medical Intelligence Article	3000 words
Special Article	2000 words
Editorial	1500 words
Book Review	750 words
Letter to the Editor	200 words
Abstract	200 words
Implications	50 words

Non-textual Material Maximum Allowance

Figure and Tables No more than 3 each or a combination of 6 total. Do not duplicate data in tables and figures. References No more than 25 references per article, up to 40 references are acceptable.

Submission of manuscripts

Manuscripts (including tables, figures, photographs,etc). accompanied by a covering letter should be signed by all the authors. The covering letter must provide an undertaking to the effect that (a) the article has not been published or submitted to or accepted for publication in any form in any other journal,(b) the authors vouch safe that the authorship of this article will not be contested by any one whose name (s) is/are not listed, (c) on acceptance the article will become copyright of AAAR (d) the sequence of the names of co-authors (e) the manuscript has been read and approved by all the authors,(f) name, address and the email ID of the corresponding author (responsible for communication).On final preparation, two hard copies and a soft copy (CD) of manuscripts should be mailed to retaining one copy with the corresponding author. A letter of acceptance or otherwise, will normally be sent to the author within 3 (three) months. Articles which are not accepted cannot be sent to the author unless accompanied by adequate postage stamps.

A completed checklist must accompany each manuscript submitted to Asian Archives of Anaesthesiology and Resuscitation.

Check the manuscript before submission

General

1. Two complete sets of manuscripts (including tables) are submitted.
2. A floppy disk or CD is submitted with two files: the complete manuscript and a separate file containing only the title page, abstract, and references.
3. Manuscript is typed double-spaced, with ample, left , justified, margins.
4. Pages are numbered consecutively, starting with the title page.

Title Page

1. On the first page are typed the title, author name(s) and major degree(s), and affiliation(s).
2. The name, address, telephone and FAX numbers, and E-mail address of the corresponding author are to be given.
3. The manuscript title is no longer than 100 characters (letters and spaces) and does not contain any abbreviations.
4. A short title (no more than 30 characters) is provided at the bottom of page for use as a running foot.
   Summary

* An abstract is provided. For all kind of articles, this abstract is structured and limited to max.300 words.

References

1. References correspond to the specifications of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals" promulgated by the International Committee of Medical Journal Editors.
2. References are identified in the text by superscript figures, eg., Miller.
3. Each reference is cited in the text. Those appearing in tables and figures should be cited in the text where the table or figure is mentioned.
4. References are numbered consecutively in the order in which they appear in the text. (Vancouver Style)
5. Unpublished data, personal communications, submitted manuscripts, statistical programs, papers presented at meetings, and non–peer-review publications are not listed in the bibliography.
6. The bibliography is typed double–spaced.
7. Abbreviations of Journal titles conform to those used in Index Medicus, National Library of Medicine.

Tables

1. Each table is typed on a separate sheet of paper with its title.
2. Tables are numbered with Arabic numerals.
3. Each table contains all necessary information in order that it may stand alone, independent of the text.
4. No table contains data that could be included in the text in several sentences.
5. Vertical lines are not used.
6. Irrelevant and extra tables must not be included

Figures

1. Each figure is cited in the text.
2. Two sets are submitted of glossy prints of sonographs, photomicrographs, radiographs, color illustrations, or any other figure that might not reproduce well.
3. Two sets of glossy prints of other figures are submitted.
4. Figures have been prepared with the journal column size in mind.
5. Letters and identifying marks are clear and sharp, and the critical areas of radiographs and photomicrographs are identified.
6. Legends and explanatory material appear in the accompanying caption and not no the figure itself.
7. Legends are typed together on one page. Legends for photomicrographs include information regarding stain and magnification.
8. Nothing is written on the back of the figures. An adhesive label, designating the top, with the first author's name and number of the figure, is attached firmly to the back of the illustration.
9. Figures are placed in a labeled envelop. No glue, paper clips or tape has been used on art.